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ATRIAL FIBRILLATION AND CHRONIC KIDNEY DISEASE

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✓ ***Resume,***

In patients with chronic kidney disease (CKD) develop bleeding and thrombotic tendencies, so the indication of anticoagulation therapy at the onset of atrial fibrillation (AF) is complex. AF is the most common chronic cardiac arrhythmia, and thromboembolism and ischemic stroke in particular are major complications.

Keywords: chronic kidney disease, atrial fibrillation, new oral anticoagulants.

ФИБРИЛЛЯЦИЯ ПРЕДСЕРДИЙ И ХРОНИЧЕСКАЯ БОЛЕЗНЬ ПОЧЕК

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✓ ***Резюме,***

У пациентов с хроническим заболеванием почек (ХБП) развиваются склонности к кровотечениям и тромбоэмболиям, поэтому показание к применению антикоагулянтов при присоединении фибрилляции предсердий (ФП) является сложным. ФП является наиболее распространенной хронической сердечной аритмией, а тромбоэмболия и ишемический инсульт, в частности, являются основными осложнениями.

Ключевые слова: хроническая болезнь почек, фибрилляция предсердий, новые оральные антикоагулянты.

БЎЛМАЧАЛАР ФИБРИЛЛЯЦИЯСИ ВА СУРУНКАЛИ БУЙРАК КАСАЛЛИГИ

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✓ ***Резюме,***

Сурункали буйрак касаллиги (СБК) бўлган беморларда қон кетишга ҳамда тромбоэмболияларга мойиллик хавфи кескин ортади, шунинг учун ҳам бўлмачалар фибрилляцияси (БФ) қўшилганда антикоагулянтларни қўллашга жуда эҳтиёткорлик билан ёндашишни талаб этади. БФ кенг тарқалган сурункали аритмиялардан бири ҳисобланади ва у кўпинча тромбоэмболия ҳамда ишемик инсультлар билан асоратланади.

Калит сўзлар: сурункали буйрак касаллиги, бўлмачалар фибрилляцияси, янги орал антикоагулянтлар.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in patients with chronic kidney disease (CKD) [1]. Moreover, in patients with CKD, AF is associated with a greater the frequency of both ischemic stroke (systemic embolism) and bleeding compared with the general population of patients with AF.

Continuous administration of oral anticoagulants is the most effective form of prevention of thrombotic complications in patients with AF. In European recommendations for the diagnosis and treatment of AF 2016 after studying the results carried out at that time direct oral anticoagulant studies (PAA)were deemed preferable to the appointment(in the absence of contraindications) than warfarin,in patients with AF and retained, as well as moderately reduced (CC 30-49 ml/min) filtration function kidneys [2].

Use of NOAC in patients with AF and concomitant CKD requires the selection of the correct doses of drugs inconnection with various renal clearance of representatives NOAC class and the need to maintain balance"Benefit / risk". However, in the literature there are practically no data on prospective studies of NOAC,as well as comparing them with AF combined with CKD. Published several sub-analyzes of the mainrandomized clinical trials (RCTs) -RE-LY, ROCKET AF, ARISTOTLE in patients with AF, depending on the degree of decrease in filtration functionkidneys [3-6]. The disadvantages of this type of data collectioncan be attributed a retrospective nature, as well as a comparison of each NOAC (rivaroxaban) with warfarin only. Also in a numberwork and clinical observations are data onthat NOAC, like warfarin, can lead to the development of anticoagulant-associated nephropathy [7]. Incurrently, to understand the efficacy and safety of using NOAC in a cohort of patients withCKD There are several studies conducted among patients with end-stage CKD, as well as studiesassessing the impact of NOAC on the progression of CKD(study XARENO, NCT02663076 [8]; RE-ELECT,NCT03789695 [9]).

The aim of our work was to evaluate the effect of oral anticoagulants (warfarin and rivaroxaban) on the filtration functionkidney in everyday clinical practice in patientswith AF, depending on the stage of CKD, and compare the effectiveness and safety of drugs with each other.

Materials and methods

We conducted a prospective single-centernon-randomized non-interventional observational study in parallel groups evaluating the effectiveness and safety of usewarfarin and available in UzbekistanNOAK (rivaroxaban)in patients with moderately reduced renal function, as well as their effect on the filtration capacity of the kidneys (median follow-up was 10 months).A total of 127 patients were included in the studywith AF: 92 with diagnosed CKD (CKD group (+)) and 35 without CKD (CKD group (-)). Average age of participantspatients amounted to 72.2 ± 8.5 years. Patients had highrisk of thrombotic complications (average 4 points ona scaleCHA2DS2-VASc) and a moderate risk of developing major bleeding (HAS-BLED average score of 1.4). Ofconcomitant pathology most often (in 96.1%) there was arterial hypertension (AH), a quarter of patients(25.2%) suffered from type 2 diabetes mellitus. Rowpatients had a history of cardiovascular events (17.3% of patients had previouslymyocardial infarction (MI), and 18.9% - ischemic strokeor transient ischemic attack (TIA)). Comparative characteristics of patients from groupsCKD (+) and CKD (-) are presented in table 1.

Table1.

Comparative characterization of patients with AF depending on the concomitant presence of CKD

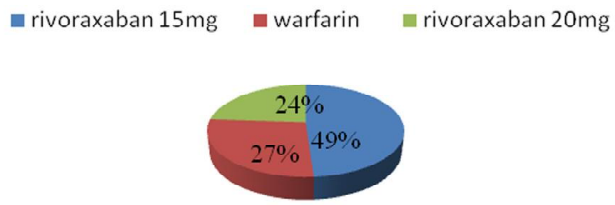
Patient characteristics	CKD(+) n-92	CKD(-) n-35	P
Men	36 (39,1%)	18 (51,4%)	0,21
Women	56 (60,9%)	17 (48,6%)	0,21
Average age, years	73,8±7,82	68,0±8,89	<0,001
Average BMI, kg/m^2	29,5±5,28	28,3±4,14	0,26
HAS-BLED average, score	1,6±0,83	1,1±0,83	<0,01
CHA_2DS_2-VASc average, score	4,3±1,47	3,1±1,48	<0,001
GFR (CKD-EPI) media, ml/min/1.73m^2	54,1±16,13	79,3±10,59	<0,001
CC (by Cocroft-Gault) med,ml/min	62,7±23,53	89,4±23,55	<0,001
Concomitant pathology			
Stroke/TIA	19 (20,7%)	5 (14,3%)	0,57
Previous MI	17 (18,5%)	5 (14,3%)	0,77
Diabetes	27 (29,3%)	5 (14,3%)	0,13
Arterial hypertension	90 (97,8%)	32 (91,4%)	0,13
CHF (FV≤40%)	9 (9,8%)	5 (8,6%)	1,00

Significant differences between the groups were obtained by age (in the CKD group (+) patients were significantly older than patients from the CKD group (-), p <0.001),the number of points on the scales CHA2DS2-VASc and HAS-BLED(in the CKD (+) group, patients had a greater risk asthrombotic and hemorrhagic events), as well asin terms of renal filtration function (GFR according toCKD-EPI and CC), which is consistent with the characteristics of patients with CKD in the population.

All patients under observation every 3months assessed the dynamics of filtrationkidney function as well as efficacy and safetyanticoagulant therapy. Depending on the anticoagulant taken, patients in the CKD (+) group were divided as follows (Fig. 1).

Figure 1.

Disposition of patients with AF and CKD to drugs and drug dosages



Most often, patients with CKD in our sample from the CKD group(+) took rivoraxaban, second in frequency of appointments(27%).Distribution of CKD Patients in a Study bythe stages are presented in table 2.

Table 2.

Disposition of patients with AF and CKD stages

CKD stages	GFR (CKD-EPI)	Number of patients
C1	>90 ml/min/1,73m^2	5 (54%)
C2	60-89 ml/min/1,73m^2	28 (30,4%)
C3a	45-59 ml/min/1,73m^2	31 (33,7%)
C3b	30-44 ml/min/1,73m^2	26 (28,3%)
C4	15-29 ml/min/1,73m^2	2 (2,2%)

In our work, patients with 3a-, 2- and 3b-stages of CKD (in total - 92.4% of the totalnumbers with AF and CKD).The initial characteristics of the filtration functionkidneys (CC, GFR) in patients with CKD taking various NOAK and warfarin did not differ significantly.

Table 3.

Comparative characterization of patients with AF and CKD depending on anticoagulant taken

Indicator	Rivoraxaban (67)	Warfarin (25)	P
Average age, years	75,7±6,61	74,4±7,82	0,155
HAS-BLED, points±SD	1,5±0,79	1,8±0,72	0,240
CHA_2DS_2-VASc, points±SD	4,3±1,49	4,2±1,46	0,143
GFR (CKD-EPI) med, ml/min/1.73m^2	56,8±18,02	51,0±17,11	0,412
CC (by Cocroft-Gault) med,ml/min	60,4±24,91	56,3±19,13	0,113

In general, patients taking different AC did not differ. However, in a pairwise comparison, patients taking warfarinwere significantly younger than patients taking rivaroxaban (p = 0.047). And in the groupwarfarin turned out to be patients with a significantly higher estimated risk of bleeding on the HAS-BLED scale,than patients in the rivaroxaban group (p = 0.036).

The initial characteristics of the filtration functionkidney (creatinine clearance and GFR) in patients with AF and CKD, depending on the drug they receive,did not differ significantly. However, a pairwise comparison showed a significant difference in QCbetween groups of patients taking warfarin andrivaroxaban: in the group receiving rivaroxaban, QC wassignificantly lower (p = 0.01).

Results

During the observation period, we did not reveal any significant changes in the filtration function of the kidneys in anyone of the groups (Fig. 2-4).

Figure 2.

Dinamics of creatinin level (mcmol/l) in patients with CKD on various oral anticoagulants

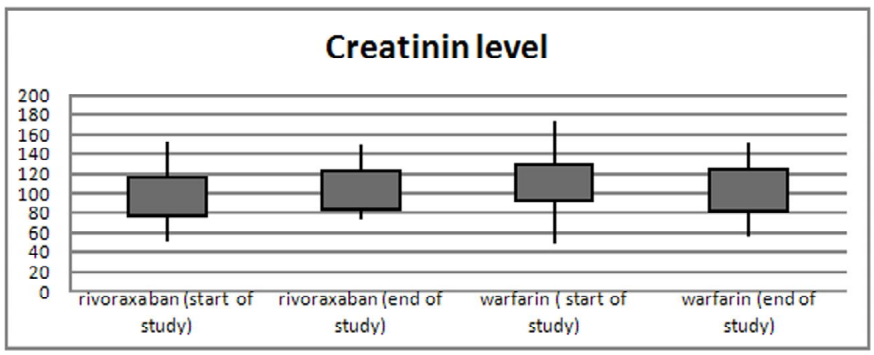


Figure 3.

Dinamics of GFR (CKD-EPI, ml/min/1.73m2) in patients with CKD on various oral anticoagulants

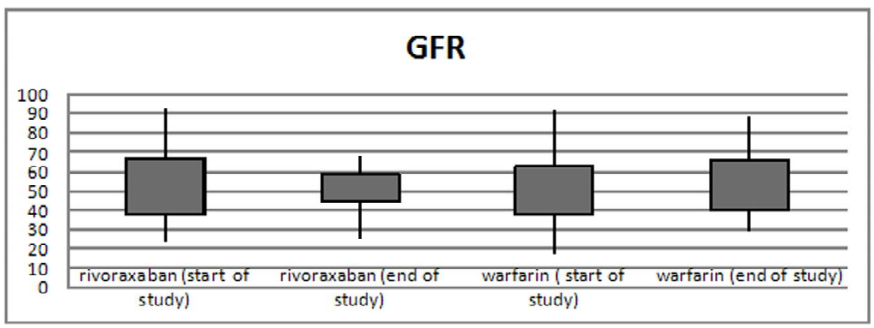
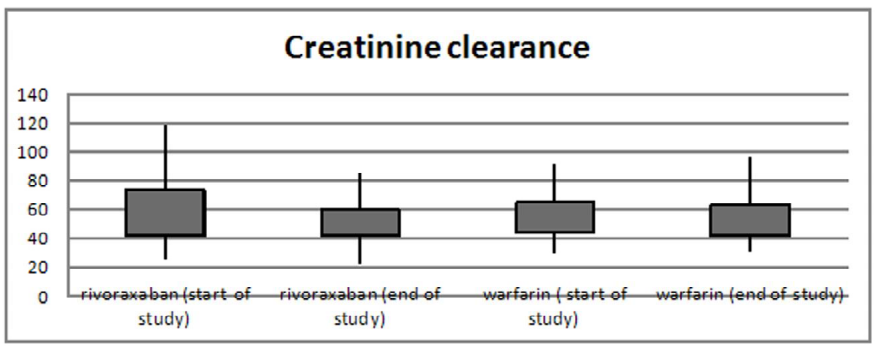


Figure 4.

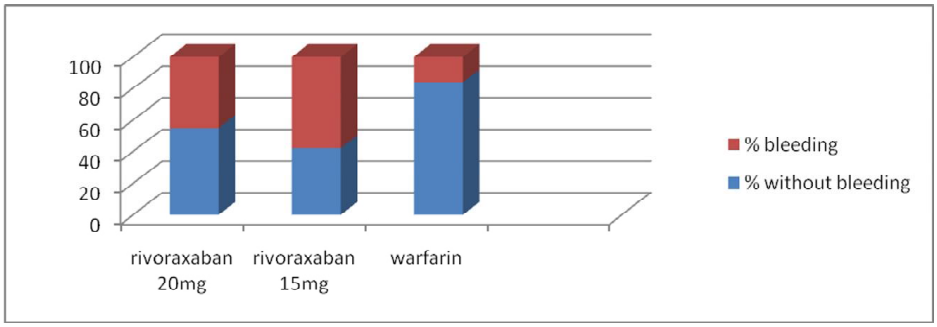
Dinamics of CC (ml/min) in patients with CKD on various oral anticoagulants



Despite the high estimated risk of thrombotic events on the scaleCHA2DS2-VASc (4.3 ± 1.47 points) ingroup of patients with CKD, we did not observe any thromboembolic complications of AF in any of the drugs, which can be explained by a not so long periodobservations. Quite significant, on the other handthe clinical fact is that for all the time of ourthere were no large cases of observation with warfarin and NOAC in patients with AF and CKDbleeding. We recorded 25 smallhemorrhagic events that did not require cancellationanticoagulant therapy (with the exception of oneminor clinically significant bleeding from a stomach ulcer, in which temporary withdrawal was performed anticoagulant with subsequent resumption of its intake). The distribution of hemorrhagic events, depending on the drug taken and its dosage, is presented in Figure 5.

Figure 5.

Bleeding rate depending on the anticoagulant and its dose in patients with AF and CKD (%)



Discussion

In a subanalysis of the study ROCKET-AF Christopher B. Fordyce Coll. also revealedgreater reduction in CC in patients receiving warfarin(-4.3 ± 14.6 ml/min) compared with patients receiving rivaroxaban (-3.5 ± 15.1 ml / min, p <0.001) [11]. The above work allowed suggest a nephroprotective effect inclass NOAC, however, the reliability of these data is limited by the retrospectiveness of their receipt.The main limitations of our studyare the lack of randomization, open characterresearch, a short observation period andlimited number of patients involved. There arethe data obtained on the differences between groups of drugs should be interpreted with caution.In any case, the role of smallbleeding due to the fact that they often become the cause of interruption / cessation of anticoagulant therapy, and this, in turn, significantly increasesthe risks of thromboembolic complications of AF, andalso an unfavorable predictor of overallmortality in patients with AF [12].

Conclusions

In general, we can conclude that the reception ofother NOAC or warfarin by patients with AF and CKD did not significantly affect the dynamics of renal filtration function, which may be related to the concomitant nephroprotective therapy obtained in a large percentage of cases. Pooh probablyhave a nephroprotective effect only relativelyComparison with Vitamin K Antagonist Therapyvarious NOAK (as well as warfarin) in patients with AFand CKD for a little less than a year was not accompanied by the development of thromboembolic complications and largebleeding, which is in favor of its effectiveness and safety. In connection with a significantly largethe number of hemorrhagic events in the backgroundwith warfarin, regardless of its dose, in patients with AF and moderate CKD, treatment with rivaroxaban can be considered preferred.

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